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SHIAO, REI TSANG	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/533,341	BARTON ET AL.	
	Examiner	Art Unit	
	Rei-tsang Shiao, Ph.D.	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 September 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10 and 14-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,9,10 and 14-16* is/are rejected.

7)☒ Claim(s) *8* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *02/28/06, 04/29/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This application claims benefit of the foreign applications: UNITED KINGDOM 0225987.7 with a filing date 11/07/2002; and UNITED KINGDOM 0310932.9 with a filing date 05/13/2003.

2. Claims 1-10 and 14-16 are pending in the application.

Information Disclosure Statement

3. Applicant's Information Disclosure Statements, filed on February 28, 2006 and April 29, 2005 have been considered. Please refer to Applicant's copies of the 1449's submitted herein.

Responses to Election/Restriction

4. Applicant's election with traverse of election of Group I claims 1-10 and 14-16, in part, in the reply filed on September 24, 2007 is acknowledged. The traversal is on the grounds that applicants believe that it would pose no additional burden on the Examiner to search Group II in addition to Group I. This is found not persuasive, and the reasons are given *infra*.

Claims 1-10 and 14-16 are pending in the application. The scope of the invention of the elected subject matter is as follows.

Claims 1-10 and 14-16, in part, drawn to compounds of formula (I), wherein the variable A independently represent carbocyclyl phenyl, or heterocyclyl selected from pyridyl, thiazolyl or pyrazinyl thereof, the variables R_1-R_5 independently do not represent

heteroaryl or heterocyclyl; the variable R_1-R_5 independently is not substituted with heteroaryl or heterocyclyl, and their methods of use.

The claims 1-10 and 14-16 herein lack unity of invention under PCT rule 13.1 and 13.2 since the compounds defined in the claims lack a significant structural element qualifying as the special technical feature that defines a contribution over the prior art, see Davies et al. CAS: 107: 58881. Davies et al. discloses similar phenylsulfonamide compounds. Accordingly, unity of invention is considered to be lacking and restriction of the invention in accordance with the rules of unity of invention is considered to be proper. Furthermore, even if unity of invention under 37 CFR 1.475(a) is not lacking, which it is lacking, under 37 CFR 1.475(b) a national stage application containing claims to different categories of invention will be considered to have unity of invention if the claims are drawn only to one of the following combinations:

(1) A product and a process specially adapted for the manufacture of said product', or

(2) A product and a process of use of said product; or

(3) A product, a process specially adapted for the manufacture of the said product, and a use of the said product; or

(4) A process and an apparatus or means specifically designed for carrying out the said process; or

(5) A product, a process specially adapted for the manufacture of the said product, and an apparatus or means specifically designed for carrying out the said process.

And, according to 37 CFR 1.475(c)

if an application contains claims to more or less than one of the combinations of categories of invention set forth in paragraph (b), unity of invention might not be present.

However, it is noted that unity of invention is considered lacking under 37 CFR 1.475(a) and (b). Therefore, since the claims are drawn to more than a product, and according to 37 CFR 1.475 (e)

> the determination whether a group of inventions is so linked as to form a single general inventive concept shall be made without regard to whether the inventions are claimed in separate claims or as alternatives within a single claim.

The claims lack unity of invention and should be limited to only a product, or a process for the preparation, or a use of the said product. In the instant case, Groups I-II are drawn to various products and methods of use, and the products of compounds of formula (I) having a moiety of phenyl or pyrazine of the variable A of Group I do not contain a common technical feature or structure of Group II, wherein the variable A represents a moiety of thienyl or furyl, and do not define a contribution over the prior art, i.e., phenylsulfonmide compounds of Davies et al. Moreover, the examiner must perform a commercial database search on the subject matter of each group in addition to a paper search, which is quite burdensome to the examiner.

Claims 1-10 and 14-16, in part, embraced in above elected subject matter, are prosecuted in the case. Claims 1-10 and 14-16, in part, not embraced in above elected subject matter, are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention.

The requirement is still deemed proper.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-7 and 14-16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described. They are:

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,
5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of the skill in the art.

In the instant case:

The nature of the invention

The nature of the invention of claims 1-7 and 14-16 is intent methods of use (i.e., inhibiting 11βHSD1 or treating diabetes) using compounds of formula (I), see claims 1 or 15.

The state of the prior art and the predictability or lack thereof in the art

The state of the prior art is that the pharmacological art involves screening *in vitro* and *in vivo* to determine which compounds exhibit the desired pharmacological activities (i.e. what compounds can treat which specific diseases by what mechanism). There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

The instant claimed invention is highly unpredictable as discussed below:

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. *In re Fisher*, 427 F.2d 833,166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

Applicants are claiming intent methods of use using compounds of formula (I) effective inhibiting 11βHSD1 or treating diabetes, which includes any disease related to 11βHSD1. As such, the specification fails to enable the skilled artisan to use the compounds of formula of (I) to treat any disease related to inhibiting 11βHSD1.

In addition, there is no established correlation between *in vitro* activity and

accomplishing treating disorders or diseases related to inhibiting 11βHSD1, *in vivo*, and those skilled in the art would not accept allegations in the instant specification to be reliable predictors of success, and those skilled in the art would not be able to use the instant compounds since there is no description of an actual method wherein any diseases related to inhibiting 11βHSD1 in a host is treated.

Hence, one of skill in the art is unable to fully predict possible results from the administration of the instant compounds of the claims due to the unpredictability of the treatment of disease related to inhibiting 11βHSD1. The diseases related to an inhibiting 11βHSD1 without limitation are known to have many obstacles that would prevent one of ordinary skill in the art from accepting treating regimen on its face.

The amount of direction or guidance present and the presence or absence of working examples

The only direction or guidance present in the instant specification is description of several references related to 11βHSD1 knock-out mice model disclosed by Kotelevtsev Y. et al, see lines 11-20 on page 2. There are no *in vitro* or *in vivo* working examples present for the treatment of any diseases by the administration of the instant compounds of formula (I) of the instant invention.

The breadth of the claims

The breadth of the claims is intent methods of use using the compounds of formula (I) effective against disease related to inhibiting 11βHSD1.

The quantity of experimentation needed

The quantity of experimentation needed is undue experimentation. One of skill in the art would need to determine what disorders related to inhibiting 11βHSD1 would be benefited (i.e., treated) by the administration of the instant compounds of formula (I) of the instant invention and would furthermore then have to determine which of the claimed methods of use using the instant compounds would provide treatment of diseases related to inhibiting 11βHSD1, if any.

The level of the skill in the art

The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by *in vitro* and *in vivo* screening to determine which compounds exhibit the desired pharmacological activity and which diseases would benefit from this activity. Thus, the specification fails to provide sufficient support of the broad use of the compounds of the instant claims for the treatment of any diseases related to inhibiting 11βHSD1. As a result necessitating one of skill to perform an exhaustive search for which diseases related to inhibiting 11βHSD1, can be treated by what methods of use of the compounds of formula (I) in order to practice the claimed invention.

Genentech Inc. v. Novo Nordisk A/S (CA FC) 42 USPQ2d 1001, states that " a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "patent protection is granted in return for an enabling

disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the Wands factors and *In re Fisher* (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in undue experimentation, with no assurance of success.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 9-10 are rejected under 35 U.S.C. 102 (b) as being anticipated by (1) Leclercq et al. CAS: 113:191296; (2) Coppola et al. CAS: 92:146570; (3) Hendrickson et al. CAS: 84:16883; (4) Albrecht's CAS: 89: 109326; (5) Davies et al. CAS: 107: 58881 or (6) Vega et al. CAS: 128:270172.

Applicants claim compounds/compositions of formula (Ia), wherein the variable A represents phenyl or pyridyl, see claim 1.

Leclercq et al. disclose a compound, see RN: 130214-77-6, it clearly anticipate the instant compounds of formula (Ia), wherein the variable A represents phenyl substituted with nitro, the variable R_2 or R_3 independently represents hydrogen or alkyl, and the variable R_4 or R_5 independently represents alkyl(i.e., methyl).

Coppola et al. disclose a compound, see RN: 73281-91-1, it clearly anticipate the instant compounds of formula (Ia), wherein the variable A represents phenyl, the variable R_2 or R_3 independently represents hydrogen or alkyl, and the variable R_4 or R_5 independently represents alkyl(i.e., methyl).

Hendrickson et al. disclose a compound, see RN: 58044-88-5, it clearly anticipate the instant compounds of formula (Ia), wherein the variable A represents phenyl, the variable R_2 or R_3 independently represents hydrogen or alkyl (i.e., methyl), and the variable R_4 or R_5 independently represents alkyl (i.e., methyl or butyl).

Albrecht's discloses two compounds, see RN: 67323-19-7 or 67323-27-7, it clearly anticipate the instant compounds of formula (Ia), wherein the variable A represents phenyl substituted with amino, nitro, or alkoxy (i.e., methoxy), the variable R_2 or R_3 independently represents hydrogen or alkyl, and the variable R_4 or R_5 independently represents alkyl(i.e., methyl).

Davies et al. discloses two compounds, see RN: 108494-90-2 or 108494-69-5, it clearly anticipate the instant compounds of formula (Ia), wherein the variable A represents phenyl substituted with amino, halo, alkylamino (i.e., methylamino), or alkoxy (i.e., methoxy), the variable R_2 or R_3 independently represents hydrogen or alkyl, and the variable R_4 or R_5 independently represents alkyl (i.e., methyl).

Vega et al. disclose a compound, see RN: 205697-22-7, it clearly anticipate the instant compounds of formula (Ia), wherein the variable A represents phenyl, the variable R_2 or R_3 independently represents hydrogen or alkyl (i.e., methyl), and the variable R_4 or R_5 independently represents alkyl (i.e., methyl).

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in Graham v. John Deere Co., 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 9-10 are rejected under 35 U.S.C. 103(a) as being obvious over Davies et al. CAS: 107: 58881.

Applicants claim compounds/compositions of formula (Ia), wherein the variable A represents phenyl or pyridyl, see claim 1.

Determination of the scope and content of the prior art (MPEP §2141.01)

Davies et al. discloses two compounds, see RN: 108494-90-2 or 108494-69-5.

Determination of the difference between the prior art and the claims (MPEP §2141.02)

The difference between the instant claims and Davies et al. is that the instant variable A represents phenyl or pyridyl, while Davies et al. represents phenyl at the same position. Davies et al. compounds overlap with the scope of the instant invention.

Finding of prima facie obviousness-rational and motivation (MPEP §2142-2143)

One having ordinary skill in the art would find the instant claims 9-10 prima facie obvious **because** one would be motivated to employ the compounds of Davies et al. to obtain the instant methods of use, wherein compounds of formula (Ia), wherein the variable A represents phenyl.

The motivation to obtain the claimed catalyst derives from known Davies et al. compounds would possess similar activities (i.e., agents for pharmaceutical compositions) to that which is claimed in the reference.

Claim Objections

8. Claims 1-10 and 14-16 are objected to as containing non-elected subject matter, i.e., carbocyclyl, heterocyclyl, thienyl, or furyl, etc. It is suggested that applicants amend the claims to the scope of the elected subject matter as defined on the pages 2-3 *supra*.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rei-tsang Shiao whose telephone number is (571) 272-0707. The examiner can normally be reached on 8:30 AM - 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph K. McKane can be reached on (571) 272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Rei-tsang Shiao, Ph.D.
Patent Examiner
Art Unit 1626

November 16, 2007